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REVIEW

The relationship between Mycoplasma and Kawasaki disease in pediatric patients: An updated systematic review and meta-analysis

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ABSTRACT

Objectives: This study aimed to clarify the relationship between *Mycoplasma pneumoniae (M. pneumoniae)* and Kawasaki disease by conducting an updated systemic review and meta-analysis of published studies.

Materials and methods: Studies mentioning *M. pneumoniae* and Kawasaki disease before October 2022 were included in this meta-analysis. The pooled prevalence was calculated, and the log odds ratio in the random effects model was applied to estimate the pooled prevalence of *M. pneumoniae* infection in pediatric patients with Kawasaki disease. In addition, the clinical parameters, such as hemoglobin and erythrocyte sedimentation rate, were analyzed. Six studies with a total of 1,859 pediatric patients with Kawasaki disease were enrolled. The focused outcome was the pooled prevalence and clinical parameters.

Results: The pooled prevalence of *M. pneumoniae* infection was statistically significant in pediatric patients with Kawasaki disease. In addition, the values of hemoglobin and erythrocyte sedimentation rate were significantly different between *M. pneumoniae*-infected and non-*M. pneumoniae*-infected patients with Kawasaki disease. Other clinical parameters were not significantly different between *M. pneumoniae*-infected and non-*M. pneumoniae*-infected patients with Kawasaki disease.

Conclusion: The results suggest that *M. pneumoniae* infection is significantly prevalent in pediatric patients with Kawasaki disease. The lower values of hemoglobin and erythrocyte sedimentation rate in *M. pneumoniae*-infected patients with Kawasaki disease might be needed to investigate further.

Keywords: Erythrocyte sedimentation rate, hemoglobin, Kawasaki disease, meta-analysis, mycoplasma, pooled prevalence.

Kawasaki disease (KD) is a self-limited vasculitis with immune function alterations and contributes to the most cases of acquired heart disease in the children of developed countries and is an important cause of long-term cardiac disease in adulthood.[1] The clinical features include erythema and cracking of lips, bilateral bulbar conjunctival injection without exudate, erythema of oral and pharyngeal mucosa enlarged cervical lymph node, strawberry tongue, erythema and edema of the hands and feet in the acute phase, skin rash, and subacute periungual desquamation.[2,3] The clinical decision-making should be based on the individual's condition and patient-specific circumstances.[4] The etiology of KD is still unknown and might be associated with some viruses. However, the relationship between the candidate viruses and KD have not been confirmed.[5] In addition, the cell damage pattern and related oxidative stress molecules might be associated with the elevated

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proinflammatory cytokines and inflammasome, which might contribute to vasculitis and the inflammatory symptoms of KD. The postinfectious inflammatory response pathophysiology of KD might also be shared with the etiology for multisystem inflammatory syndrome for children.[6,7] The laboratory parameters of several indicators have been mentioned in the differential diagnosis and clinical monitoring of KD,[8] such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), hemoglobin, white blood cell (WBC), and neutrophil percentage.

Mycoplasma pneumoniae contributes to 10 to 40% of community-acquired pneumonia in children and is a common pathogen for respiratory tract infections.[9] *M. pneumoniae* infection is a significant cause of hospitalization in the pediatric patients, particularly for children younger than six years old without typical clinical manifestations of pneumonia signs.[10] In addition, *M. pneumoniae* infection is prone to have a longer course of illness within the community-acquired pneumonia.[11] The coinfection of *M. pneumoniae* and other viruses might contribute to a more severe course of community-acquired pneumonia.[11,12] Therefore, the *M. pneumoniae* infection should be well investigated in the pediatric population.

For the comorbidity of pediatric KD and *M. pneumoniae* infection, the previous studies found around 10 to 22% incidence of *M. pneumoniae* infection in pediatric KD patients.[13-15] According to the literature above, pediatric KD patients are prone to heart disease, and *M. pneumoniae* infection contributes to most community-acquired pneumonia. The comorbidity of KD and *M. pneumoniae* infection might contribute to the more severe complications of the heart and lung in pediatric patients. The sequelae should be crucial for the clinical management of pediatric patients. In addition, there are still many unanswered questions of KD, particularly the comorbidity of *M. pneumoniae* infection and KD. Therefore, we conducted this systematic review and meta-analysis to confirm the relationship between pediatric KD and *M. pneumoniae* infection. In addition, the laboratory parameters were compared between a *M. pneumoniae*-infected group and a non-*M. pneumoniae* infection group of pediatric KD patients to establish any significant difference in the laboratory parameters.

MATERIALS AND METHODS

Literature search and selection criteria

The following keywords were used to search and collect the related articles in PubMed, Science Direct, EmBase, Web of Science, and the Cochrane Central Register of Controlled Trials (CENTRAL): "Mycoplasma," "Kawasaki disease," "infection," "positive," "negative," "pediatric," "children," "hemoglobin," "erythrocyte sedimentation rate," "C-reactive protein," "*Mycoplasma pneumoniae*" or "outcome," "comparison," "versus," "incidence," "prevalence," "white blood cell," and "platelet." The search was limited to the literature published or electronically published online before October 2022. The inclusion criteria for studies were as follows: *(i)* studies with data of *M. pneumoniae* infection and number of KD patients; *(ii)* comparisons between an *M. pneumoniae*-infected subgroup and a subgroup of patients with infections other than *M. pneumoniae* (the non-*M. pneumoniae* infection group) of KD patients; *(iii)* studies with detailed data of outcome in the perspective of infection, such as CRP, ESR, WBC, and neutrophil percentage; *(iv)* studies with detailed data on blood analyses, including hemoglobin, WBC, and platelets; *(v)* studies published in the journals of science citation index database in the English language. Consequently, six studies with a total of 1,859 pediatric patients with Kawasaki disease were included in the analyses.

Quality assessment and data extraction

We followed the Cochrane Handbook for Systematic Reviews and Interventions to conduct this meta-analysis. In addition, the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guideline was used for reporting our meta-analysis results.[16] The following data were collected from the enrolled studies. First, the *M. pneumoniae* infection event and number of patients with KD. Second, the non-*M. pneumoniae* infection event and number of pediatric patients with KD. Third, the CRP, ESR, WBC, and neutrophil

percentage of the *M. pneumoniae*-infected subgroup and the non-*M. pneumoniae* infection subgroup of pediatric KD patients. Fourth, the hemoglobin and platelet of the *M. pneumoniae*-infected subgroup and the non-*M. pneumoniae* infection subgroup of pediatric KD patients.

Data extraction and critical appraisal

Two reviewers assessed the abstracts, selected the articles, and then independently evaluated the full-text version of the selected studies. Afterward, the two reviewers independently extracted the focused data from the text, tables, and figures of the enrolled articles. The enrolled articles had data on the event and number of *M. pneumoniae* infections, detailed data on outcome in the perspective of infection (CRP, ESR, WBC, and neutrophil percentage), detailed data on outcome in the perspective of hematological parameters (hemoglobin, WBC, and platelet) in the full-text content. A collaborative review was conducted by all authors to achieve a strong agreement (kappa=0.8). All authors also reviewed the final results.

Meta-analysis and statistical analysis

The Cochrane Collaboration Review Manager (RevMan) software version 5.4 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, 2022) was used to perform the meta-analyses. For pooled prevalence of *M. pneumoniae* infection in KD, we generated pooled estimates of log odds ratios (ORs), along with the associated standard error (SE). Due to the lack of patient-level data, we used summary statistics for each study by extracting the reported ORs. In studies without ORs and SEs, we calculated these parameters according to the published data from each individual study for subsequently obtaining an estimate of ORs and SEs. The data was transformed to the log ORs using the ORs and SEs in the Rev Man calculation function. The risk estimates of individual studies were combined via the inverse variance-weighted averages of log ORs in the random-effects model. The risk estimates of individual studies were combined via the variance-weighted averages in the random-effects model. In addition, the random and fixed effects models were used with inverse variance function-weighted log ORs. The log OR results were used to determine if the prevalence of *M. pneumoniae* infection was significant in KD.

For continuous variables, the weighted mean difference was used to estimate numerical variables. The *M. pneumoniae*-infected and non-*M. pneumoniae* infection subgroups were compared to find if there was any significant difference for WBC, neutrophil percentage, CRP, ESR, platelet, and hemoglobin. The overall effect size of WBC, neutrophil percentage, CRP, ESR, platelet, and hemoglobin was calculated as the weighted average of the inverse variance for the study-specific estimates. The chi-square test was used to study heterogeneity between enrolled studies. The derived estimate of heterogeneity *(I^2)* was used to estimate statistical heterogeneity of studies included in the meta-analysis.[17] Based on the Cochrane Handbook, the random effects model was used in the current meta-analysis. All *p* values were two-sided. Publication bias was assessed using a funnel plot test. A *p* value <0.05 was considered statistically significant.

RESULTS

Enrollment of studies

The PRISMA flow diagram of the current meta-analysis is demonstrated in Figure 1. The qualitative analysis of the remaining six articles was performed, and the remaining six studies were included in the quantitative analysis.[13-15,18-20] The characteristics of the enrolled six studies are summarized in Table 1.

Log OR of M. pneumoniae-infected versus non-*M. pneumoniae*-infected pediatric patients with KD

The I^2 was 100%, which suggested a high heterogeneity in the sample of enrolled studies in this perspective. The test for overall effect was Z=2.70 (p=0.007), and the meta-analysis results showed a significant difference of log OR of *M. pneumoniae*-infected versus non-*M. pneumoniae*-infected pediatric patients with KD under random effects model. The results favored the *M. pneumoniae*-infected status in pediatric patients with KD (Figure 2).

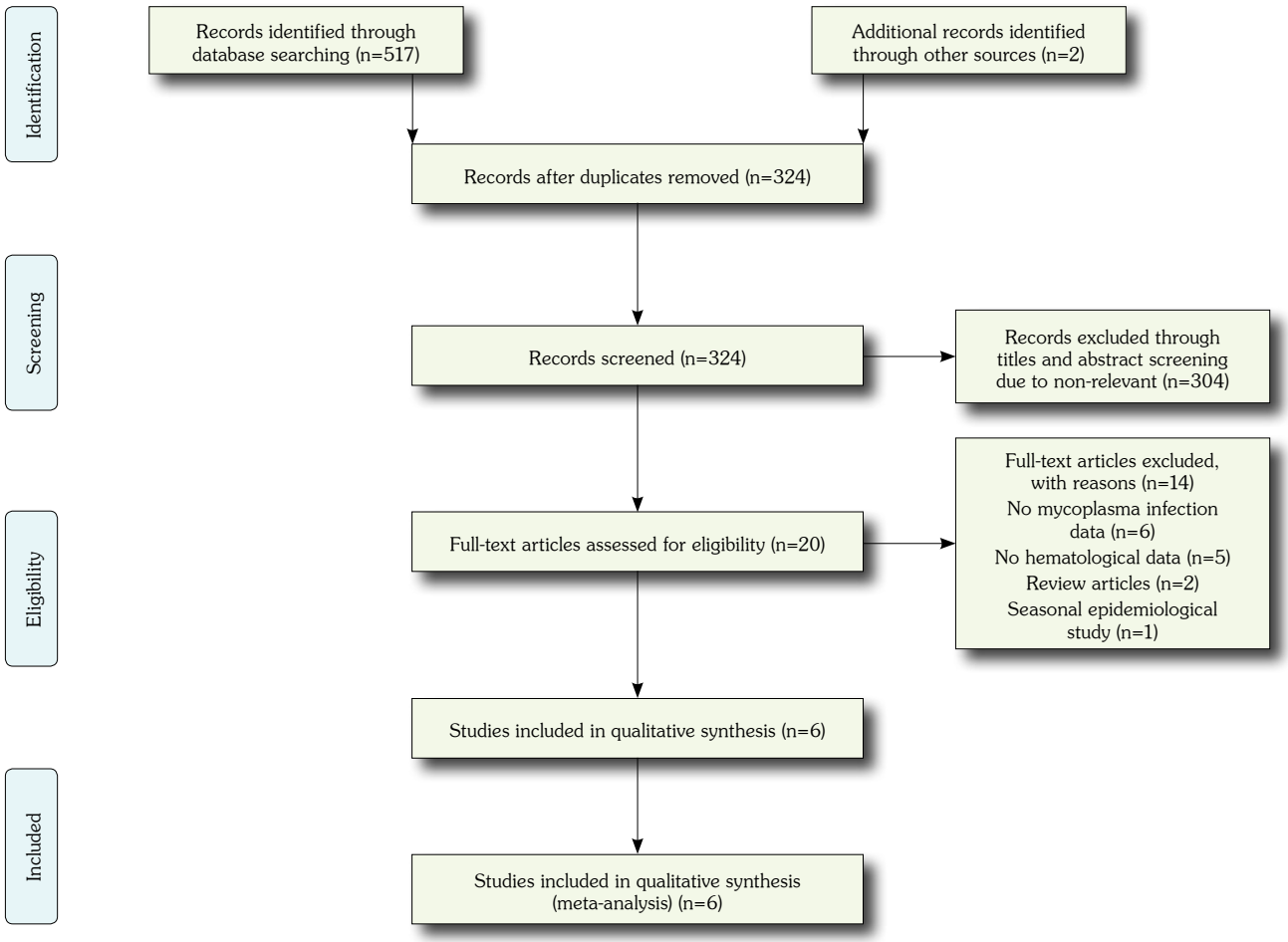

Figure 1. PRISMA flow chart for the selection of enrolled studies.

The meta-analysis results for ESR in the comparison between *M. pneumoniae*-infected and non-*M. pneumoniae*-infected pediatric patients with KR.

The standardized mean difference between the *M. pneumoniae*-infected group and the non-*M. pneumoniae* infection group was 0.34 (95% CI: 0.07-0.62) in the random effects model, which suggested that the ESR of *M. pneumoniae*-infected group of pediatric KD patients was higher than that of the non-*M. pneumoniae* infection group of pediatric KD patients (test for overall effect Z=2.47, p=0.01). A significant heterogeneity was also noted [Tau2=0.03, Chi2=3.69, degree of freedom (df)=2 (p=0.16), I^2=46%] (Figure 3).

The meta-analysis results for hemoglobin in the comparison between *M. pneumoniae*-infected and non-*M. pneumoniae*-infected pediatric patients with KD

The standardized mean difference between the *M. pneumoniae*-infected group and the non-*M. pneumoniae* infection group was 0.45 (95% CI: 0.03-0.86) in the random effects model, which suggested that the hemoglobin of *M. pneumoniae*-infected group of pediatric KD patients was higher than that of the non-*M. pneumoniae* infection group of pediatric KD patients (test for overall effect Z=2.12, p=0.03). A significant heterogeneity was noted [Tau2=0.09, Chi2=6.11, df=2 (p=0.05), I^2=67%] (Figure 4).

Table 1. Summary of enrolled studies

	Patients	Inclusion criteria	MP detection and evaluation	Outcome
Ding 2021 (Single center, China)	Male: 493 (57%) Median age: 21 months) MP detection number: 420 MP infection number: 81 Non-MP infection number: 339	KD diagnosed by Japanese Kawasaki Disease Research Committee before 2017 and by the American Heart Association after 2017	Serology and PCR findings. Both the presence of IgM antibodies and positive PCR results were used as sufficient criteria for current MP infection	The incidence of KD The incidence of MP infection among KD patients (before and after COVID-19 pandemic outbreak)
Lan 2020 (Single center, China)	Retrospectively analyzed 210 pediatric patients with KD complicated with pneumonia. 97 MP infection 113 non-MP infection	Inclusion of KD was based on criteria defined by American Heart Association	MP IgM antibodies or respiratory samples by PCR with positive results for MP	MP incidence In KD patients CRP, ESR, WBC neutrophil percentage hemoglobin platelet, cytokine albumin
Lee 2011 (Single center, South Korea)	12 MP infection KD patients (mean age: 5.5±3.5 years) 42 non-MP infection KD patients (mean age: 2.8±2.2 years)	Inclusion of KD was based on criteria defined by American Heart Association	Serum anti-MP antibody (AMA) titer in patients with KD serologic tests with elevated single titers (>1:640) or a fourfold rise in titer	MP incidence in KD patients CRP, ESR, WBC neutrophil and lymphocyte percentage hemoglobin platelet, albumin echocardiography chest radiography
Park 2017 (Single center, South Korea)	37 MP-infection KD patients (mean age: 48.2±32.1 month; 67.6% male) 115 non-MP infection KD patients (mean age: 31.7±21.7 months; 58.3% male)	Inclusion of KD was based on criteria defined by American Heart Association	Anti-MP IgM ≥1:640 or an increase in anti-MP IgG by more than 4-fold in consecutive tests between 10 to 21 days	MP incidence in KD patients CRP, WBC hemoglobin pro-brain natriuretic peptide clinical symptoms coronary artery lesion
Tang 2016 (Single center, China)	62 MP infection KD patients (median: 25 months; 64.5% male) 388 non-MP infection KD patients (median age 14.5 months; 65.6% male)	Inclusion of KD was based on criteria defined by American Heart Association	Serology and PCR findings. (IgM antibodies positive PCR results) as sufficient criteria for current MP infection	MP incidence in KD patients CRP, ESR, WBC neutrophil and lymphocyte percentage hemoglobin platelet clinical symptoms
Tang 2016a (Single center, China)	82 MP infection KD patients 187 non-MP infection KD patients	Inclusion of KD was based on criteria defined by American Heart Association	Serology and PCR findings	Coronary artery Lesions MP incidence

MP: Mycoplasma pneumoniae; KD: Kawasaki disease; PCR: Polymerase chain reaction; IgM: Immunoglobulin M; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; WBC: White blood cells; IgG: Immunoglobulin G.

Nonsignificant results

The standardized mean differences of WBC, neutrophil percentage, CRP, and platelet were not significantly different between the *M. pneumoniae*-infected group and the non-*M. pneumoniae* infection group in the random effects model.

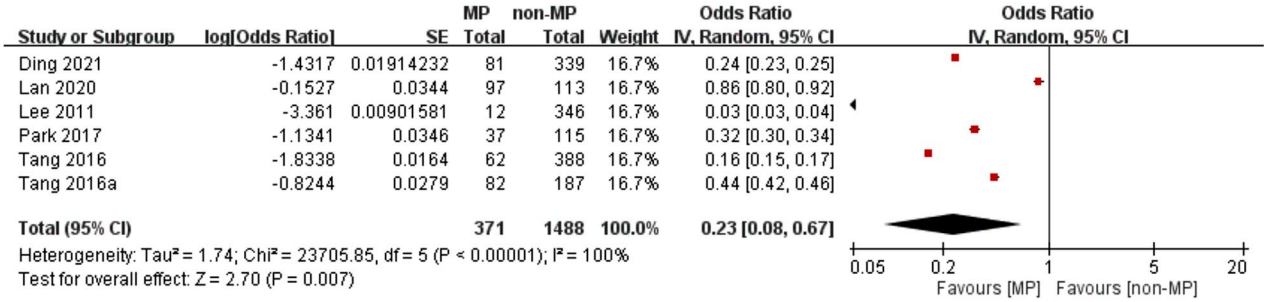

Figure 2. The forest plot of log OR for the meta-analysis results of pediatric patients with KD [*M. pneumoniae* infection vs. non-*M. pneumoniae* infection].

MP: Mycoplasma pneumoniae; CI: Confidence interval; SE: Standard error; OR: Odds ratios; KD: Kawasaki disease.

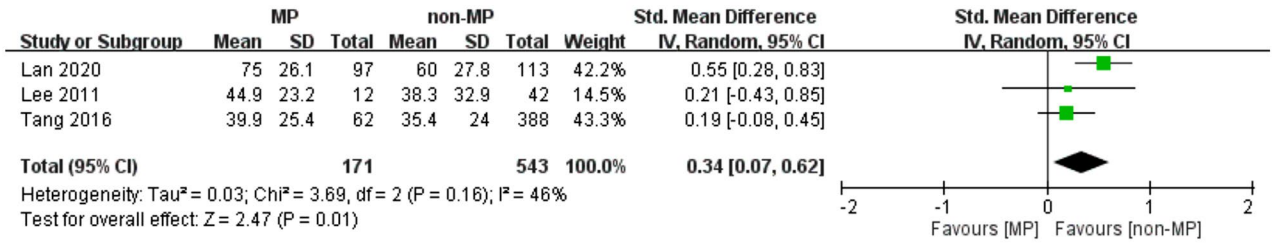

Figure 3. The forest plot for the meta-analysis results of ESR in pediatric KD patients [*M. pneumoniae* infection vs. non-*M. pneumoniae* infection].

MP: Mycoplasma pneumoniae; SD: Standard deviation; CI: Confidence interval; KD: Kawasaki disease.

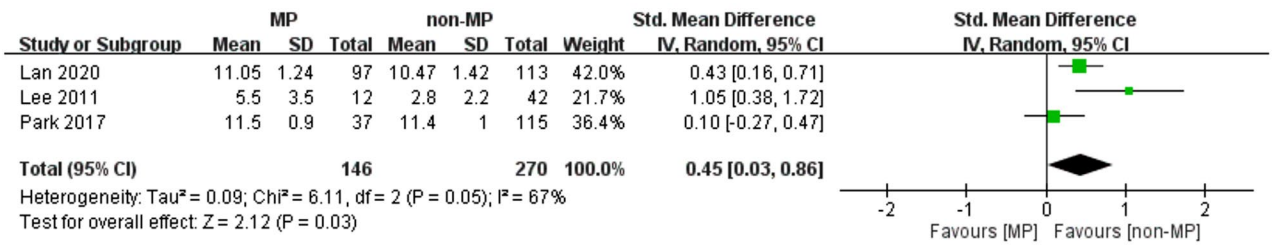

Figure 4. The forest plot for the meta-analysis results of hemoglobin in pediatric KD patients [*M. pneumoniae* infection vs non-*M. pneumoniae* infection].

MP: Mycoplasma pneumoniae; SD: Standard deviation; CI: Confidence interval; KD: Kawasaki disease.

DISCUSSION

In the current meta-analysis, we found that the *M. pneumoniae*--infected group was significantly different from the non-*M. pneumoniae* infection group in the log OR of event number in pediatric patients with KD. It suggested that *M. pneumoniae* infection might be significantly associated with pediatric KD compared to non-*M. pneumoniae* infections. Apart from the significant association of *M. pneumoniae* infection and pediatric KD, the infection and hematological parameters might be the potentially differentiating points between *M. pneumoniae* infection and non-*M. pneumoniae* infection in pediatric KD patients. Our meta-analytic results found that ESR and hemoglobin were significantly different between the *M. pneumoniae*-infected group and the non-*M. pneumoniae* infection group. It showed that *M. pneumoniae* infection might be associated with a significantly higher value of ESR compared to non-*M. pneumoniae* infections. In addition, *M.*

pneumoniae infection might have a significantly higher value of hemoglobin compared to non-*M. pneumoniae* infections. The results suggest that *M. pneumoniae* infection might be a distinct group of pediatric KD compared to non-*M. pneumoniae* infections. To our knowledge, this is the first meta-analysis study focused on a *M. pneumoniae*-infected subgroup of pediatric KD patients. The results of the current meta-analysis can provide valuable information for clinicians to focus more on pediatric KD patients with an *M. pneumoniae* infection. According to the obtained data, the cut-off values of abnormal ESR and hemoglobin levels might be undetermined due to the relatively low number of enrolled studies and variable range of ESR and hemoglobin of enrolled studies. Therefore, we recommend that pediatric clinicians examine complete blood count, CRP, and ESR in pediatric KD patients. If the elevated ESR and hemoglobin are noted without the abnormality of WBC, neutrophil percentage, CRP, and platelet count, pediatric clinicians should be vigilant about the possibility of a comorbid *M. pneumoniae* infection.

The incidence of *M. pneumoniae* infection in pediatric KD patients is around 10 to 22% in the enrolled studies.[15,18,20] However, the comparison between *M. pneumoniae* infection and non-*M. pneumoniae* infections in the log OR of pooled prevalence has not been published in a previous study. In the current meta-analysis, the significant log OR of *M. pneumoniae* infection might represent that it might be significantly prevalent in pediatric KD patients. The comorbidity of KD and *M. pneumoniae* infection in pediatric patients should be cautioned in clinical practice, and clinical treatment due to the predisposing characteristics of immune function alterations in pediatric KD. The early treatment should be performed in pediatric KD comorbid with *M. pneumoniae* infection due to the concern of original immune function alterations of pediatric KD patients.[13,15]

The alterations of hemoglobin and ESR have been reported in previous studies of *M. pneumoniae* infection. A study reported that severe *M. pneumoniae* infection might be associated with significant differences in hemoglobin and ESR. In addition, the study suggested that ESR might be an indicator among a combination of laboratory parameters to predict the severe form of *M. pneumoniae* infection.[21] The *M. pneumoniae* infection of pediatric KD patients might lead to a more severe tendency due to the predisposing trait of immune function alterations in pediatric KD patients. Therefore, the hemoglobin and ESR might be important indicators to identify the *M. pneumoniae* infection in pediatric KD patients. A recent study also mentioned that hemoglobin values might be significantly different between *M. pneumoniae* infection and other groups of infection in pediatric patients.[22] Another study of severe *M. pneumoniae* infection also suggested that ESR values could be decreased after the medication treatment.[23] ESR has also been reported to be associated with the target protein expression of *M. pneumoniae* infection in pediatric patients.[24] ESR values were also higher in pediatric patients with refractory *M. pneumoniae* infection, which suggested the predictive value of this biomarker for *M. pneumoniae* infection in pediatric patients.[25] One of the enrolled studies also supported that the higher value of ESR might occur in *M. pneumoniae*-infected pediatric KD patients.[14] Another enrolled study suggested that clinicians should alter their approach in pediatric KD patients with a higher value of ESR, which might be associated with *M. pneumoniae* infection.[13] A previous study also supported the crucial role of ESR in the prediction of refractory subtype of *M. pneumoniae* infection.[26] The elevation of ESR might be one of the clinical phenomenon of *M. pneumoniae* infection.[27] The increase of ESR might suggest an increase in positively charged proteins and a decrease in negatively charged albumin in *M. pneumoniae*-infected pediatric KD patients.[28] In the current meta-analysis, the *M. pneumoniae*-infected group did not have significantly higher values of CRP compared to the non-*M. pneumoniae* infection group of pediatric KD patients. It also corresponded to the previous study suggesting that ESR and CRP were different biomarkers and should be used in a context-dependent way.[28] ESR has a longer half-life than CRP. Therefore, ESR might be useful for monitoring chronic inflammatory condition,[29-31] such as the *M. pneumoniae* infection of pediatric KD patients. The elevation of hemoglobin and ESR might represent a potential type of biomarker for pediatric KD

patients with *M. pneumoniae* infection under the impression of current meta-analysis results. However, a further, well-designed study in this perspective might be warranted to confirm this potential biomarker.

There were several limitations in the current meta-analysis. First, the enrolled studies were limited in sample size, and the total sample size in the current meta-analysis was still limited. Therefore, a large-scale study with a bigger sample size might be needed in the future. Second, the enrolled studies were retrospective or cross-sectional, not prospective or longitudinal. Therefore, a bias might not be avoidable under the current design of the meta-analysis and might alter the interpretations of our meta-analysis results. Future meta-analyses in this field can include prospective and longitudinal studies, which can decrease the bias and provide a more accurate viewpoint on *M. pneumoniae* infection in pediatric KD. Third, the low sample size of enrolled studies in several significant outcomes, such as ESR and hemoglobin, might limit the interpretations of the significant results. In addition, the moderate heterogeneity of significant results in the ESR and hemoglobin might be a concern issue. Fourth, the lack of patient-level data might also influence the interpretations of our results due to lack a full evaluation for patient-level covariates in across comparisons. It is impossible to confirm a possible subgroup effect related to patient age due to lack of patient-level data and limited number of enrolled studies. Fifth, a high heterogeneity was noted in the significant results of log OR of *M. pneumoniae*-infected versus non-*M. pneumoniae*-infected pediatric KD patients. This heterogeneity issue suggested that we should take the interpretation of our meta-analytic results with this issue as a consideration. Sixth, the definition and detection of *M. pneumoniae* infection are variable in the enrolled studies, which might influence the results. Finally, the lack of sex distribution and a variable age range in the months of age for pediatric KD patients in some enrolled studies might be another concern.

In conclusion, the results suggest that *M. pneumoniae* infection is significantly prevalent in pediatric patients with KD. The lower values of hemoglobin and ESR in *M. pneumoniae*-infected patients with KD might be needed to investigate further.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Research idea and study design: ZG and CM; data acquisition: Z.G., C.M.; Data analysis/interpretation: Z.G., C.M.; Statistical analysis: G.L., Z.B.; Supervision or mentorship: Z.B.; All authors takes responsibility that this study has been reported honestly, accurately and transparently, and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved.

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REFERENCES

1. de Graeff N, Groot N, Ozen S, Eleftheriou D, Avcin T, Bader-Meunier B, et al. European consensus-based recommendations for the diagnosis and treatment of Kawasaki disease - the SHARE initiative. Rheumatology (Oxford) 2019;58:672-82. doi: 10.1093/rheumatology/key344.
2. Burney JA, Roberts SC, DeHaan LL, Shimizu C, Bainto EV, Newburger JW, et al. Epidemiological and clinical features of Kawasaki disease during the COVID-19 pandemic in the United States. JAMA Netw Open 2022;5:e2217436. doi: 10.1001/jamanetworkopen.2022.17436.
3. Morishita KA, Goldman RD. Kawasaki disease recognition and treatment. Can Fam Physician 2020;66:577-9.
4. McCrindle BW, Rowley AH, Newburger JW, Burns JC, Bolger AF, Gewitz M, et al. Diagnosis, treatment, and long-term management of Kawasaki disease: A scientific statement for health professionals from the American Heart Association. Circulation 2017;135:e927-99. doi: 10.1161/CIR.0000000000000484.
5. Kuo HC, Yang KD, Chang WC, Ger LP, Hsieh KS. Kawasaki disease: An update on diagnosis and treatment. Pediatr Neonatol 2012;53:4-11. doi: 10.1016/j.pedneo.2011.11.003.
6. Hara T, Yamamura K, Sakai Y. The up-to-date pathophysiology of Kawasaki disease. Clin Transl Immunology 2021;10:e1284. doi: 10.1002/cti2.1284.
7. McCrindle BW, Manlhiot C. SARS-CoV-2-related inflammatory multisystem syndrome in children: Different or shared etiology and pathophysiology as Kawasaki disease? JAMA 2020;324:246-8. doi: 10.1001/jama.2020.10370.

8. Seo YM, Kang HM, Lee SC, Yu JW, Kil HR, Rhim JW, et al. Clinical implications in laboratory parameter values in acute Kawasaki disease for early diagnosis and proper treatment. Korean J Pediatr 2018;61:160-6. doi: 10.3345/kjp.2018.61.5.160.
9. Harris M, Clark J, Coote N, Fletcher P, Harnden A, McKean M, et al. British Thoracic Society guidelines for the management of community acquired pneumonia in children: Update 2011. Thorax 2011;66 Suppl 2:ii1-23. doi: 10.1136/thoraxjnl-2011-200598.
10. Gordon O, Oster Y, Michael-Gayego A, Marans RS, Averbuch D, Engelhard D, et al. The clinical presentation of pediatric Mycoplasma pneumoniae infections-a single center cohort. Pediatr Infect Dis J 2019;38:698-705. doi: 10.1097/INF.0000000000002291.
11. Otheo E, Rodríguez M, Moraleda C, Domínguez-Rodríguez S, Martín MD, Herreros ML, et al. Viruses and Mycoplasma pneumoniae are the main etiological agents of community-acquired pneumonia in hospitalized pediatric patients in Spain. Pediatr Pulmonol 2022;57:253-63. doi: 10.1002/ppul.25721.
12. Li F, Zhang Y, Shi P, Cao L, Su L, Fu P, et al. Mycoplasma pneumoniae and adenovirus coinfection cause pediatric severe community-acquired pneumonia. Microbiol Spectr 2022;10:e0002622. doi: 10.1128/spectrum.00026-22.
13. Lan Y, Li S, Yang D, Zhou J, Wang Y, Wang J, et al. Clinical characteristics of Kawasaki disease complicated with Mycoplasma pneumoniae pneumonia: A retrospective study. Medicine (Baltimore) 2020;99:e19987. doi: 10.1097/MD.0000000000019987.
14. Tang Y, Yan W, Sun L, Huang J, Qian W, Hou M, et al. Kawasaki disease associated with Mycoplasma pneumoniae. Ital J Pediatr 2016;42:83. doi: 10.1186/s13052-016-0292-1.
15. Lee MN, Cha JH, Ahn HM, Yoo JH, Kim HS, Sohn S, et al. Mycoplasma pneumoniae infection in patients with Kawasaki disease. Korean J Pediatr 2011;54:123-7. doi: 10.3345/kjp.2011.54.3.123.
16. Knobloch K, Yoon U, Vogt PM. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement and publication bias. J Craniomaxillofac Surg 2011;39:91-2. doi: 10.1016/j.jcms.2010.11.001.
17. Cumpston MS, McKenzie JE, Welch VA, Brennan SE. Strengthening systematic reviews in public health: Guidance in the Cochrane Handbook for Systematic Reviews of Interventions, 2nd edition. J Public Health (Oxf) 2022;44:e588-92. doi: 10.1093/pubmed/fdac036.
18. Ding YY, Ren Y, Qin J, Qian GH, Tang YJ, Chen Y, et al. Clinical characteristics of Kawasaki disease and concurrent pathogens during isolation in COVID-19 pandemic. World J Pediatr 2021;17:263-71. doi: 10.1007/s12519-021-00431-2.
19. Park HR, Han MY, Yoon KL, Cha SH, Moon SK, Jung HW. Mycoplasma infection as a cause of persistent fever after intravenous immunoglobulin treatment of patients with Kawasaki disease: Frequency and clinical impact. Infect Chemother 2017;49:38-43. doi: 10.3947/ic.2017.49.1.38.
20. Tang Y, Gao X, Shen J, Sun L, Yan W. Epidemiological and clinical characteristics of Kawasaki disease and factors associated with coronary artery abnormalities in east China: Nine years experience. J Trop Pediatr 2016;62:86-93. doi: 10.1093/tropej/fmv077.
21. Chang Q, Chen HL, Wu NS, Gao YM, Yu R, Zhu WM. Prediction model for severe mycoplasma pneumoniae pneumonia in pediatric patients by admission laboratory indicators. J Trop Pediatr 2022;68:fmac059. doi: 10.1093/tropej/fmac059.
22. Wang W, Li SH. Use of common blood parameters for the differential diagnosis of childhood infections. PLoS One 2022;17:e0273236. doi: 10.1371/journal.pone.0273236.
23. Fang C, Mao Y, Jiang M, Yin W. Pediatric critical illness score, clinical characteristics and comprehensive treatment of children with severe mycoplasma pneumoniae pneumonia. Front Surg 2022;9:897550. doi: 10.3389/fsurg.2022.897550.
24. Li W, Ding X, Zhao R, Xiong D, Xie Z, Xu J, et al. The role of targeted regulation of COX11 by miR-10a-3p in the development and progression of paediatric mycoplasma pneumoniae pneumonia. J Thorac Dis 2021;13:5409-18. doi: 10.21037/jtd-21-710.
25. Qi X, Sun X, Li X, Kong D, Zhao L. Significance changes in the levels of myocardial enzyme in the child patients with Mycoplasma Pneumoniae Pneumonia. Cell Mol Biol (Noisy-le-grand) 2020;66:41-5.
26. Lu A, Wang C, Zhang X, Wang L, Qian L. Lactate dehydrogenase as a biomarker for prediction of refractory mycoplasma pneumoniae pneumonia in children. Respir Care 2015;60:1469-75. doi: 10.4187/respcare.03920.
27. Lu A, Wang L, Zhang X, Zhang M. Combined treatment for child refractory Mycoplasma pneumoniae pneumonia with ciprofloxacin and glucocorticoid. Pediatr Pulmonol 2011;46:1093-7. doi: 10.1002/ppul.21481.
28. Umemura H, Fukuda Y, Miyashita T, Nakayama T. Elucidation of the mechanism and significance of the erythrocyte sedimentation rate from clinical laboratory data. Acta Med Okayama 2022;76:447-55. doi: 10.18926/AMO/63904.
29. Litao MK, Kamat D. Erythrocyte sedimentation rate and C-reactive protein: How best to use them in clinical practice. Pediatr Ann 2014;43:417-20. doi: 10.3928/00904481-20140924-10.
30. Bray C, Bell LN, Liang H, Haykal R, Kaiksow F, Mazza JJ, et al. Erythrocyte sedimentation rate and C-reactive protein measurements and their relevance in clinical medicine. WMJ 2016;115:317-21.
31. Costenbader KH, Chibnik LB, Schur PH. Discordance between erythrocyte sedimentation rate and C-reactive protein measurements: Clinical significance. Clin Exp Rheumatol 2007;25:746-9.